

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

Claims 1-38 (Canceled)

Claim 39 (Currently amended) A method of analyzing a first nucleic acid sample comprising:

providing said first nucleic acid sample;

reproducibly reducing the complexity of said first nucleic acid sample to produce a second nucleic acid sample by fragmenting said first nucleic acid sample to produce fragments using a selected fragmentation method comprising fragmentation with a selected restriction enzyme, ligating adaptor sequences to said fragments, and amplifying at least some of said fragments ligated with said adaptor sequences using a selected amplification method;

providing a nucleic acid array, wherein a computer system is used

(i) to query a sequence database to identify the sequence and size of the fragments that are predicted to result from digestion of the first nucleic acid sample with said selected restriction enzyme

(ii) to select a subset of said fragments that are within a selected size range and

(iii) to identify known polymorphisms present on fragments in said subset of fragments, and

wherein the probes of the array were selected to be complementary to polymorphisms identified in (iii) to identify polymorphisms that are predicted to be present on fragments that are amplified when the first nucleic acid sample is fragmented by said selected fragmentation method and amplified by said selected amplification method and the probes of the array consist essentially of probes to interrogate the genotype of a plurality of said polymorphisms;

hybridizing said second nucleic acid sample to said array; and

analyzing a hybridization pattern resulting from said hybridization.

Claim 40 (Previously presented) The method of claim 39 wherein said second nucleic acid sample comprises at least 0.5 % of the fragments in said first nucleic acid sample.

Claim 41 (Previously presented) The method of claim 39 wherein said second nucleic acid sample comprises at least 3 % of the fragments in said first nucleic acid sample.

Claim 42 (Previously presented) The method of claim 39 wherein said second nucleic acid sample comprises at least 12 % of the fragments in said first nucleic acid sample.

Claim 43 (Previously presented) The method of claim 39 wherein said second nucleic acid sample comprises at least 50 % of the fragments in said first nucleic acid sample.

Claim 44 (Previously presented) The method of claim 39 wherein said first nucleic acid sample is DNA.

Claim 45 (Previously presented) The method of claim 39 wherein said first nucleic acid sample is genomic DNA.

Claim 46 (Previously presented) The method of claim 39 wherein said first nucleic acid sample is cDNA derived from RNA or mRNA.

Claim 47 (Previously presented) The method of claim 39 wherein the steps of fragmenting said first nucleic acid sample to produce fragments, ligating adaptor sequences to said fragments, and amplifying at least some of said fragments ligated with said adapter sequences are performed in a single reaction vessel.

Claim 48 (Previously presented) The method of claim 39 wherein said step of fragmenting said first nucleic acid sample comprises digestion with at least one restriction enzyme.

Claim 49 (Previously presented) The method of claim 39 wherein said step of fragmenting said first nucleic acid sample comprises digestion with a type IIIs endonuclease.

Claim 50 (Previously presented) The method of claim 39 wherein said adaptor sequences comprise PCR primer template sequences.

Claim 51 (Previously presented) The method of claim 39 wherein said adaptor sequences comprise tag sequences.

Claim 52 (Previously presented) The method of claim 39 wherein said method for analyzing a first nucleic acid sample comprises determining whether the first nucleic acid sample contains sequence variations.

Claim 53 (Previously presented) The method of claim 52 wherein said sequence variations are single nucleotide polymorphisms (SNPs).

Claim 54-56 (Canceled)

Claim 57 (Previously presented) A method of analyzing a first nucleic acid sample comprising:
providing a first nucleic acid sample;
obtaining a second nucleic acid sample by:
binding oligonucleotide probes containing a desired SNP sequence to magnetic beads to form probe-bead complexes;
hybridizing said probe-bead complexes to said first nucleic acid sample to form target-probe complexes comprising DNA targets hybridized to complementary oligonucleotide probes, wherein the target-probe complexes comprise a double stranded portion and single stranded DNA target regions;

exposing said target-probe complexes to a single strand DNA nuclease to remove said single stranded DNA target regions thereby obtaining double stranded DNA duplexes;

ligating a double stranded adaptor sequence comprising a restriction enzyme site to said double stranded DNA duplexes to obtain adaptor-ligated DNA duplexes;

digesting said adaptor-ligated DNA duplexes with a restriction enzyme to release the magnetic bead from the adaptor-ligated DNA duplex; and

generating said second nucleic acid sample by isolating the adaptor-ligated DNA duplexes released from the magnetic beads by digestion;

providing a nucleic acid array;

hybridizing said second nucleic acid sample to said array; and

analyzing a hybridization pattern resulting from said hybridization.

Claim 58 (Previously presented) The method of claim 57 wherein said restriction enzyme is a type IIs endonuclease.

Claims 59-173 (Canceled)

Claim 174 (Previously presented) A method for genotyping a plurality of single nucleotide polymorphisms from a genomic DNA sample comprising:

(a) mixing said genomic DNA sample with a plurality of oligonucleotide probes, wherein each probe comprises a single nucleotide polymorphism and, wherein the probes are attached to beads, under conditions that allow formation of complexes comprising oligonucleotide probes bound to complementary genomic DNA target sequences;

(b) adding a single strand DNA nuclease to the complexes to remove single strand overhangs from the complexes, generating double stranded DNA duplexes attached to beads;

(c) ligating a first adaptor comprising a type IIS restriction enzyme recognition site to the DNA duplexes;

(d) digesting the duplexes with a type IIS restriction enzyme to separate the beads from the portion of the duplex containing the single nucleotide polymorphism;

- (e) ligating a second adaptor to the portion of the duplex containing the single nucleotide polymorphism;
- (f) amplifying the portion of the duplex containing the single nucleotide polymorphism to generate amplified fragments;
- (g) hybridizing the amplified fragments to an array of probes comprising allele specific probes complementary to said plurality of single nucleotide polymorphisms to generate a hybridization pattern; and
- (h) analyzing said hybridization pattern to determine the genotype of each single nucleotide polymorphism in said plurality of single nucleotide polymorphisms.

Claim 175 (Previously presented) The method of claim 174 wherein said beads are magnetic beads.

Claim 176 (Previously presented) The method of claim 174 wherein said beads are glass beads.

Claim 177 (Previously presented) The method of claim 174 wherein the genomic DNA sample is fractionated genomic DNA.